Compensation of Disabled Organogeneses in Genetically Modified Pig Fetuses by Blastocyst Complementation.

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Public Summary:
Generation of functional organs from pluripotent stem cells (PSCs) is one of the ultimate goals of regenerative medicine. Although the stem cell technology has advanced, reconstitution of three-dimensional organ in a dish is still unfeasible. An alternative approach, blastocyst complementation has been proposed. This strategy uses an empty organ niche in an animal body as a bio-incubator in which human cell occupies to create an organ. Recent studies have been demonstrated compelling evidence for blastocyst complementation in rodents by generating organs, such as kidney, brain, vessels, and blood. To fulfill the ultimate aim of generating human organs in an animal body, the use of large animals is essential. We have previously established a concept of developing exogenic pancreas in a genetically modified pig fetus with an apancreatic trait, thereby proposing the possibility of in vivo generation of functional human organs in xenogenic large animals. In this study, we aimed to demonstrate a further proof-of-concept of the compensation for disabled organogeneses in pig, including pancreatogenesis, nephrogenesis, hepatogenesis, and vasculogenesis. These dysorganogenetic phenotypes could be efficiently induced via genome editing of the cloned pigs. Induced dysorganogenetic traits could also be compensated by allogenic blastocyst complementation, thereby proving the extended concept of organ regeneration from exogenous pluripotent cells in empty niches during various organogeneses. These results suggest that the feasibility of blastocyst complementation using genome-edited cloned embryos permits experimentation toward the in vivo organ generation in pigs from xenogenic pluripotent cells.

Scientific Abstract:
We have previously established a concept of developing exogenic pancreas in a genetically modified pig fetus with an apancreatic trait, thereby proposing the possibility of in vivo generation of functional human organs in xenogenic large animals. In this study, we aimed to demonstrate a further proof-of-concept of the compensation for disabled organogeneses in pig, including pancreatogenesis, nephrogenesis, hepatogenesis, and vasculogenesis. These dysorganogenetic phenotypes could be efficiently induced via genome editing of the cloned pigs. Induced dysorganogenetic traits could also be compensated by allogenic blastocyst complementation, thereby proving the extended concept of organ regeneration from exogenous pluripotent cells in empty niches during various organogeneses. These results suggest that the feasibility of blastocyst complementation using genome-edited cloned embryos permits experimentation toward the in vivo organ generation in pigs from xenogenic pluripotent cells.